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EXAMINER
MUSTO, N

ART UNIT	PAPER NUMBER
1818	

DATE MAILED: 05/05/97

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

08/776,190

Applicant(s)

H.P. Josel et al.

Examiner

Neal A. Musto

Group Art Unit

1818



☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-38 is/are pending in the application.

Of the above, claim(s) 31-38 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-30 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims 1-38 are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 3

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 1-30, drawn to a conjugate, a process for making and using said
5 conjugate, classified in class 530, subclass 807.
 - II. Claims 31 and 32, drawn to methods of detecting an analyte, classified in class
435, subclass 7.94.
 - III. Claims 33 and 34, drawn to methods of detecting an analyte, classified in class
435, subclass 7.94.
 - 10 IV. Claims 35-38, drawn to a method of detecting a specific antibody, classified in
class 435, subclass 7.1.
2. The inventions are distinct, each from the other because of the following reasons:

The inventions of Groups I and (II, III, IV) represent separate and distinct
methods. They differ with respect to their ingredients, method steps and final result.
15 They therefore have different issues regarding patentability and enablement and
represent patentably distinct subject matter.

The inventions of Groups II, III and IV represent separate and distinct methods.
They differ with respect to their ingredients, method steps and final result. They

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therefore have different issues regarding patentability and enablement and represent patentably distinct subject matter.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, in addition to their recognized divergent subject matter, they represent an undue burden on the examiner and restriction for examination purposes as indicated is proper.

4. During a telephone conversation with Robert Murray on 8 April 1997 a provisional election was made with traverse to prosecute the invention of group I, claims 1-30. Affirmation of this election must be made by applicant in responding to this Office action. Claims 31-38 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

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Claim Objections

6. Claims 4-20 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, for the sake of compact prosecution, the claims have been treated as if dependant on claims 1 or 2.

7. Claims 25 and 26 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, for the sake of compact prosecution, the claims have been treated as if dependant on claim 21 or 22.

8. Claims 27-30 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, for the sake of compact prosecution, the claims have been treated as if dependant on claims 1 or 2.

Claim Rejections - 35 USC § 112

Claims 27-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 27-30 provides for the use of conjugates of claim 1, but, since the claim does not set forth any steps involved in the method/process, it is unclear what

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method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 27-30 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, *i.e.*, results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 22 recites the limitation "a peptide carrier" in line 3. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1, 3, 5, 6, 7, 9, 11, 12, 13, 15, 16 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Dattagupta *et al* [Dattagupta, et al., 1988].

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Dattagupta *et al* disclose a conjugate comprising a polymeric carrier conjugated with multiple fluorescein molecules (*i.e.*, both a marker and a hapten), wherein the monomeric units are nucleotides. Further, the carrier comprises a double stranded nucleic acid of 72 to 1353 monomeric units. This reads on the instant claims 1, 3, 5, 6, 7, 9, 11, 12, 13, 15, 16 and 17, which are drawn to conjugates comprising a polymeric carrier, 1-10 hapten molecules and 1-10 marker or solid phase binding groups, and the monomeric units are nucleic acids of 3-80 monomeric units.

11. Claims 2-6, 11, 12 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Bredehorst *et al* [**Bredehorst *et al.* 1991**].

Bredehorst *et al* disclose a conjugate comprising a polymer of 21 amino acids (*viz.*, insulin) which contains 3 hapten (*viz.*, fluorescein) and one solid-phase binding group (*viz.*, DNP/ anti-DNP). This conjugate is used in a competitive immunoassay. This reads on the instant claims 2-6, 11, 12, 16, and 27-29 directed to conjugates comprising a polymeric carrier 1-10 hapten molecules and 1-10 marker or solid phase binding groups, and the monomeric units are amino acids used in a competitive immunoassay.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. Claims 8, 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Dattagupta *et al* [Dattagupta, et al., 1988], in view of Bredehorst *et al* [Bredehorst *et al.* 1991], and further in view of Nielsen *et al* [Nielsen, et al., 1996].

Dattagupta *et al* and Bredehorst *et al* teach the use of polymeric carriers comprising monomeric units of either nucleotides (Dattagupta *et al*) or amino acids (Bredehorst *et al*) along with haptens and marker groups. They do not teach the use of peptide nucleic acids as a polymeric carrier molecule.

However, Nielsen *et al* teach a novel class of polymeric compounds known as peptide nucleic acids, which are naturally occurring DNA bases attached to a peptide backbone, thereby having hybrid properties of nucleic acids and peptides. Thus, it would have been *prima facie* obvious to a person having ordinary skill in the art at the time the invention was made to produce to polymeric carriers as taught by Dattagupta *et al* and Bredehorst *et al*, in the format of peptide nucleic acids as taught by Nielsen *et al*, because greater degree of flexibility in the types of polymeric units that can serve as carriers. Therefore, one of ordinary skill in the art at the time the invention was made would be motivated to do so since one would have a wide choice of carrier molecules..

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14. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bredehorst *et al* [Bredehorst *et al.* 1991], in view of Gadow *et al* [Gadow, et al., 1987]. Bredehorst *et al* teaches a conjugate comprising a polymer of 21 amino acids (viz., insulin) which contains a hapten/solid phase binding group (viz., DNP) and several reporter groups (viz., fluorescein). This conjugate is used in a competitive immunoassay for DNP and is used to detect the presence of antibody to DNP. They do not teach the use of luminescent metal chelates as marker groups.

However, Gadow *et al* teach the use of luminescent metal chelate as marker with better properties (*i.e.*, enhanced sensitivity) for immunological assays. Thus, it would have been *prima facie* obvious to a person having ordinary skill in the art at the time the invention was made to employ the luminescent metal chelate as taught by Gadow *et al* in the conjugates taught by Bredehorst *et al* because of their greater sensitivity. Thus one of ordinary skill in the art at the time the invention was made would be motivated to do so since it was known in the art that luminescent metal chelate were advantageous due to their ability to enhance sensitivity.

15. Claims 21, 23, 24, are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith *et al* [Smith, et al., 1989]. Smith *et al* teach methods for the synthesis of oligonucleotides which contain one or more free aliphatic amino groups attached to the

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nucleoside monomeric units. This permits selective placing of amino groups at any position on oligonucleotide of any composition or length, wherein a variety of moieties (viz., biotin, fluorescein) can be attached to the amino groups to yield a modified oligonucleotide.

5 However, it would have been *prima facie* obvious to a person having ordinary skill in the art at the time the invention was made to produce to claimed polymeric carriers using the methods taught by Smith *et al* because of the ease and versatility of the disclosed methods. Thus one of ordinary skill in the art at the time the invention was made would be motivated to do so since the method of Smith *et al* was well
10 establish and commercially supported by reagents.

16. Claims 22, 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lelievre *et al* [**Lelievre, et al., 1995**].

Lelievre *et al* teach the production of a 14 amino acid peptide labeled with biotin and 4-azido-salicylic acid. These haptens/binding group were introduced post-
15 synthetically to primary amino groups in a sequential manner, by selective cleavage of protecting groups. They do not teach per se the first and second protecting groups selected from acid-stable and acid labile. However, it would have been *prima facie* obvious to a person having ordinary skill in the art at the time the invention was made to chose dissimilar chemistries for bi-derivatization because of the selectivity inherent.
20 Therefore, one of ordinary skill in the art at the time the invention was made would be

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motivated to do so since it was known that di-derivatization could be accomplished using opposing protective agents as taught by Lelievre *et al.*

17. Claims 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bredhorst *et al* [**Bredehorst *et al.* 1991**] in view of Smith *et al* [**Smith, et al., 1989**].

5 Bredehorst *et al* teach a conjugate comprising a polymer of 21 amino acids (*viz.*, insulin) which contains 3 hapten (*viz.*, fluorescein) and one solid-phase binding group (*viz.*, DNP/ anti-DNP). This conjugate is used in a competitive immunoassay for DNP and is used to detect the presence of antibody to DNP. They do not teach the production of the conjugate via solid phase synthesis using monomeric units.

10 However, Smith *et al* teach methods for the synthesis of oligonucleotides which contain one or more free aliphatic amino groups attached to the nucleoside monomeric units. This permits selective placing of amino groups at any position on oligonucleotide of any composition or length, wherein a variety of moieties (*viz.*, biotin, fluorescein) can be attached to the amino groups to yield a modified oligonucleotide.

15 Thus, it would have been *prima facie* obvious to a person having ordinary skill in the art at the time the invention was made to use the conjugated carriers as taught by Bredehorst *et al* produced by the method taught by Smith *et al* because of the greater latitude in the polymeric matrix offered by de novo synthetic techniques. Therefore, one of ordinary skill in the art at the time the invention was made would be motivated
20 to do so since one would have a greater spectrum of carriers than just insulin.

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18. Claims 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bredehorst *et al* [**Bredehorst *et al.* 1991**], in view of Berzofsky et al [**Berzofsky, et al., 1989**].


Bredehorst *et al* teaches a conjugate comprising a polymer of 21 amino acids (viz., insulin) which contains a hapten/solid phase binding group (viz., DNP) and several reporter groups (viz., fluorescein). This conjugate is used in a competitive immunoassay for DNP and is used to detect the presence of antibody to DNP. They do not teach the use of haptens of the type disclosed in the instant claims (viz., oligopeptide/peptide nucleic acids or oligonucleotides).

However, Berzofsky et al teaches that haptens may comprise single antigenic determinate that are small organic compounds including oligosaccharides (*i.e.*, DNA) or oligopeptides. Thus, it would have been *prima facie* obvious to a person having ordinary skill in the art at the time the invention was made to use carriers containing haptens as taught by Bredehorst *et al*, with the haptens such as oligopeptides or oligonucleotides, because it is known that these may serve as haptens (Berzofsky et al) and one would want to broaden the specificity of the carriers to include haptens of a wide variety thereby broadening the range of assays for which the carriers could be used. Therefore, one of ordinary skill in the art at the time the invention was made would be motivated to do so since it was known in the art that there are advantages to

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using diverse haptens such as oligopeptides or oligonucleotides, for example diversity of immunological specificity.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Neal A. Musto, Ph.D. whose telephone number is (703) 305-4505. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Donald E. Adams, Ph.D. can be reached at (703) 308-0570. The fax phone number for Group 1800 is (703) 305-7939 or (703) 308-4242. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1800 receptionist whose telephone number is (703) 308-0196.


DONALD E. ADAMS
SUPERVISORY PATENT EXAMINER
GROUP 1800

Neal A. Musto, Ph.D.
FN087761.1
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